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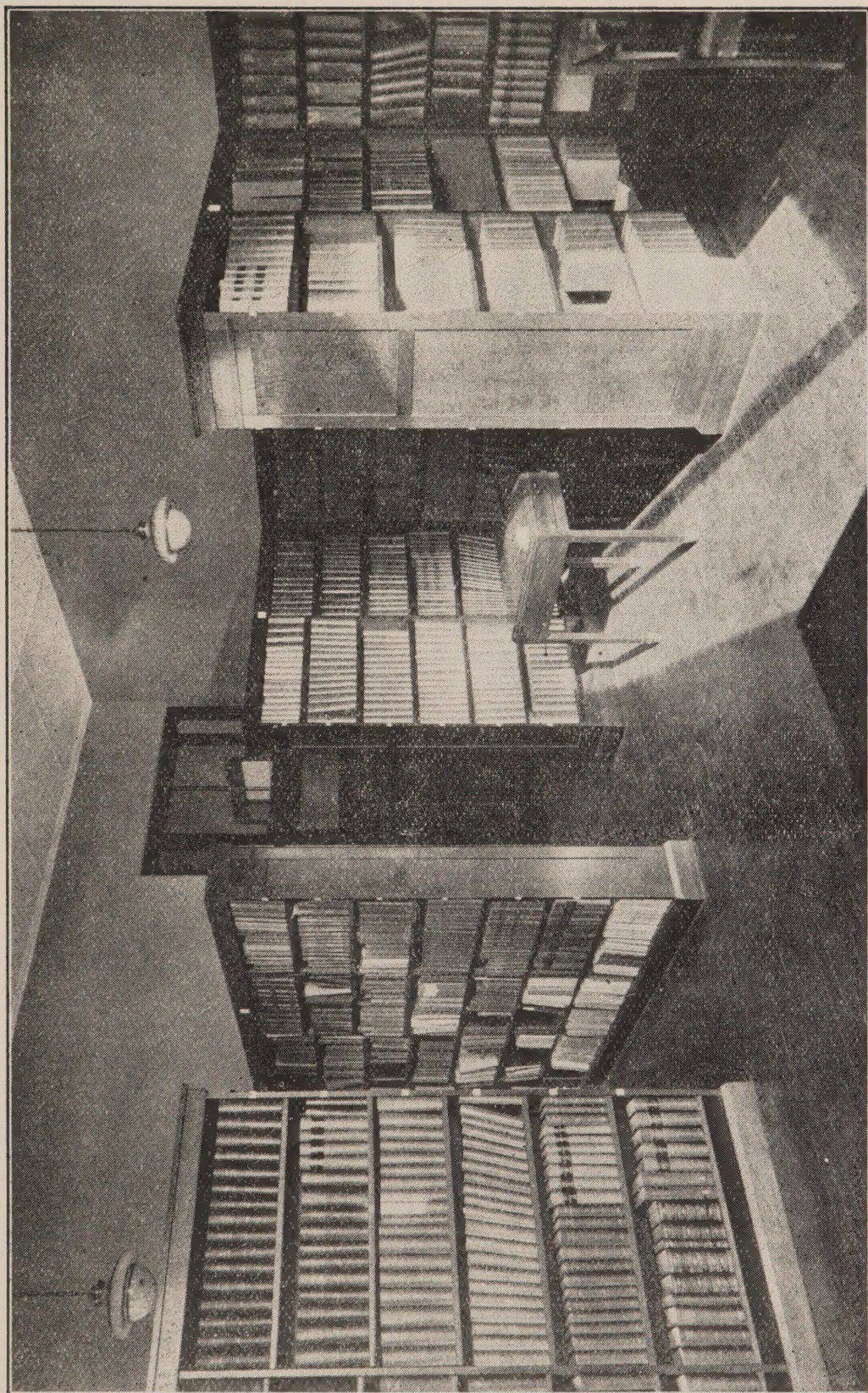
THE WALTER AND ELIZA HALL
INSTITUTE
OF RESEARCH IN
PATHOLOGY AND MEDICINE



TENTH
ANNUAL REPORT
1928-29.



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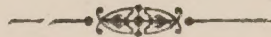
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1928-29

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TENTH
ANNUAL REPORT
1928-29.

Melbourne :

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1929.

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MISS BERYL SPLATT, B.Sc. (MELB.), Bio-Chemist.

MISS CECIL MAUDSLEY, B.Sc. (MELB.).

MISS JEAN BROAD, B.Sc. (MELB.).

Sir George Syme, who only a few months earlier had assumed the Presidency of the Hospital and the Chairmanship of the governing board of this Institute, died after a brief illness on April 19th. As a senior member of the Staff of the Hospital, Sir George had had much to do with the beginnings of the Institute, and was keenly interested in its progress and in its close relation to the Hospital. His death is a great loss to us, for he brought to the chairmanship of the board not only all the wealth of his ripe experience, but an intimate knowledge of our special problems.

The Tenth Annual Report

OF THE

Walter and Eliza Hall Institute of Research

July, 1929.

This year the work of the Institute has been consolidated and expanded. This has been largely due to assistance from the Commonwealth Department of Health, from which a grant of £4,000 has been received. This grant is being expended on researches on the Australian snake venoms, on staphylococcal and streptococcal infections, on hydatid disease and on poliomyelitis.

The Edward Wilson (The Argus) Trust have continued to assist our biochemical department, and their gift of £1,000 for this year has enabled us to continue and develop this part of our activities. It is hoped that in the near future the Endowment Fund instituted by the late Sir Aaron Danks may be increased sufficiently to provide permanent income for the upkeep of the department.

The Felton Bequest Committee has also generously helped us again this year.

Dr. N. H. Fairley's departure for England in December last was a great loss to us. He was working at the Institute for nearly two years—for the first part of this time in an honorary capacity. Later he postponed his return to England for a year to carry out certain researches for the Commonwealth Department of Health. These researches on Australian snake venoms, on hydatid disease,

on bilharzia, and on the incidence of some diseases of the domestic herbivora will be dealt with in detail later in this report. Apart from the large amount of work for which Dr. Fairley was personally responsible, and his capacity for organisation as displayed in several of these researches, we shall miss most of all the inspiration of his presence with us.

Miss Margot McKie joined the staff in August as Bacteriological Research Fellow. She is assisting Dr. F. M. Burnet in his work on the staphylococci.

Miss Eileen Kennedy took over the charge of our media department in January.

The post of Secretary to the Director and Librarian was filled in August by the appointment of Mr. Southwood, who was formerly Assistant Registrar in the University of Bristol. Mr. Southwood's experience in administration and office work has already proved of great value to us.

The Work of the Institute.

Australian Snake Venoms.

This work was inaugurated by Dr. N. H. Fairley and has been carried out on behalf of the Department of Health of the Commonwealth Government. It falls naturally into two parts—(a) the collection of venom for use in research and for the preparation of antivenine at the Commonwealth Serum Laboratories, and (b) researches on the Australian poisonous snakes and their venoms.

(a) The Collection of Venom.

This was organised by Dr. N. H. Fairley, and is now being carried on by Dr. Kellaway. Owing to the kindness of the President, Council and Director of the Zoological Gardens, we have been able to house our reptiles and collect the venom there. We have also been permitted to take into our service Mr. T. Eades, who was in charge of the reptile house, and who is now wholly employed by us in the collection of snakes and their care. We have expended £300 in enlarging the reptile house, and the premises, though not entirely suitable for this work, are greatly improved. During this season Mr. Eades has made collecting trips to Mount Gambier (2), to Tintaldra (2), and to Western Queensland (2).

Our thanks are particularly due to Mr. K. J. MacKinnon, of Tintaldra, to Mr. Kirby, of Mingbool Station, Mt. Gambier, and to Mr. W. Winter Irving, for placing at our disposal facilities for collection of snakes. Since November last we have collected venom from 25 black snakes, 120 tiger snakes, 80 copper heads, and 104 death adders. Between the beginning of November and the end of May we procured 10 grams of dried tiger snake venom, 8 grams of copper head venom, 2 grams of black snake venom and 11 grams of death adder venom.

The venom is collected by making the snakes bite through a piece of thin sheet rubber stretched across a medicine glass, the reserve venom being expressed manually by pressure on the glands. The venom obtained in this way is free from saliva. The rubber covering is slit with scissors and the venom is dried *in vacuo* for 48 hours over sulphuric acid or calcium chloride.

The snakes are milked and fed every three weeks. An interval of at least a week is allowed between milking and feeding, so that the reptiles may have sufficient venom for digestion.

Snakes collected early in the season do not live long in captivity—possibly because they have not had time to get fit and well fed after their winter sleep. There is still much room for improvement in the care of snakes in captivity under the conditions which obtain here. An attempt to provide sufficient ultra violet radiation for the reptiles has been made by placing “vita glass” in fan lights in the roof of the new house.

Many of the snakes are heavily infested with fluke when they are captured, and some die from this cause. Ideally all the snakes, with the possible exception of the death adders, would be best housed in the open air in a pit similar to that advocated by Brazil and used at the Butantan Institute.

Recently we have adopted the method of forcibly feeding our reptiles with a mixture of eggs and milk. This has been necessary owing to the difficulty of procuring sufficient supplies of natural food. The additions to our houses were made at the end of the summer, and it was thought that the heating apparatus would be adequate for the additions as well as for the old houses. This proved not to be the case, and our yields of venom fell off greatly in the autumn. Owing to the generosity of Mr. J. M. Niall, Mr.

W. Winter Irving and Mr. K. J. MacKinnon, we have been able to instal a new boiler, and the temperature conditions in the reptile houses are now thoroughly satisfactory.

For the supplies of the venoms of the Cobra and Russell vipers we are indebted to Lt.-Col. Mackie, who has kindly sent us a further supply from the Haffkine Institute, Bombay. By the kindness of Mr. R. J. Kinghorn and Mr. Donald Thomson we have also procured samples of the venom of the large elapine snake found in Northern Queensland by Maclellennan and described by Kinghorn as *Oxyuranus maclellennani*.

We have also obtained venom from one or two rare snakes which have been captured by Mr. T. Eades, and which will later be investigated.

Venom is being supplied to Dr. Morgan at the Commonwealth Serum Laboratories, where for some months horses have been injected to immunise them with tiger snake and death adder venoms. This year immunisation against copper head venom has also been commenced there.

One of the difficulties attendant upon the application of serum therapy is that the sera appear to be strictly specific. There is bound to be some uncertainty in regard to the snake responsible for any particular case of snake bite, since in some instances the same snake goes by different names in different localities, and in others the same name is applied to quite different reptiles. To overcome these difficulties Dr. Kellaway, with Mr. T. Eades, is preparing some field notes on the common venomous snakes, giving details of their distribution and habits, and discussing their differentiation. At present there appears to be no possibility of making polyvalent antivenine, but it is hoped that antivenine will be distributed in accordance with the distribution of the reptiles. Accurate information is now being gathered in regard to this, and our thanks are due to Mr. L. Glauert, Curator of the Western Australian Museum, to Mr. J. Kershaw, Curator of the National Museum, Melbourne, to Mr. J. R. Kinghorn, Curator of the reptilian collection at the Australian Museum, Sydney, to Mr. Heber Longman, Director of the Queensland Museum, and to Mr. Clive Lord, Director of the Tasmanian Museum, for kindly giving us valuable particulars of distribution in Australia and Tasmania.

Undoubtedly the most important cause of fallacious responses in the skin test is infestation with other helminths. Skin tests with extracts of *T. saginata* and *Ascaris lumbricoides* showed that patients sensitised with these extracts could react with scolex extract. Patients who had been operated on for hydatid disease, and who gave positive immediate reactions with scolex extracts in 74% of cases, gave reactions with *T. saginata* and ascaris in 59% and 23% of cases respectively. On the other hand there were nearly 30% of positive intradermal responses with ascaris extract in a series of patients with no evidence of hydatid disease, and of nine patients with recent or old infestation with thread worms none reacted with either *T. saginata* extract or hydatid fluid. Infestation with tapeworms may, therefore, cause sensitiveness to hydatid fluid and scolex extracts, but infestation with nematodes is a much less likely source of error.

Among the 35 patients who showed fallacious positive immediate reactions there was one with a history of angio-neurotic oedema and three with a recent history of urticaria. *Urticaria factitia*, which, according to Lewis, occurs in 5% of normal people, must be excluded. *Jaundice*, as a cause of pseudopositive reaction, does not appear to be so important as was earlier thought.

More exacting standards and controls for the test are laid down. The antigen used for the test should be standardised by being used on a series of patients in whom there is no evidence of hydatid disease, and on a patient known to show both phases of the response with a suitable hydatid antigen. Standard measurements should be adopted for positive, doubtful and negative results.

The stroke test, introduced by Lewis to determine the reaction of the superficial tissues to slight trauma, should be used as a routine control in all cases tested. No significance should be attached to an immediate reaction occurring in any patient showing a triple response to the stroke test, nor in one who shows a positive or doubtful reaction to the control injection of normal saline solution.

If these tests show that the patient is a suitable subject for the test, a positive immediate or delayed reaction should not be interpreted as a genuine one until infestation with other helminths has been excluded.

minutes. It is, therefore, necessary to apply a ligature and excise the bite at once. Ligature should be applied round a portion of the limb which contains a single bone; for example, round the arm in bites of the upper limb. It should be tied on the heart side of the bite, and should be tight enough to completely obstruct the circulation. The question of the efficiency of ligature is discussed fully in a later paper in the series. In regard to excision Fairley advocates excision of an area of skin and subcutaneous tissue surrounding the bite 3.2 x 1.9 c.m. ($1\frac{1}{4}$ x $\frac{3}{4}$ inch) with the longest diameter through the line joining the fang punctures. In bites of the hand and foot dissection should be down to the bone, and in other regions should be deeper than the length of the fangs—i.e., 5 or 6 mm. ($\frac{1}{4}$ inch). The wound may be swabbed with 5% permanganate solution and an Esmarch bandage applied from the ligature downward may be of value. The ligature should be left on for 20 or 30 minutes at least after excision. Finally, Dr. Fairley puts the case for the intravenous administration of antivenine in the light of its proved value in other countries. Though the number of cases of snake bite in Australia and the resulting mortality is small, there is no reason why this wastage of human life should not be avoided.

The second paper, also by Dr. N. H. Fairley, deals with the dentition and biting mechanism of the Australian venomous snakes. A new method of studying the dentition of the reptiles has been applied—namely, that of taking impressions of the bite in dental wax and subsequent reconstruction in casts to determine the exact position of the fang during biting. In this reconstruction work Dr. Fairley had the assistance of Dr. Mason Cox, D.D.Sc. The alteration in the position of the fang was also studied in snakes by electrical stimulation of the biting musculature after the destruction of the brain by pithing. The impressions of the bite provided a ready method of measuring the distance between the fangs and of determining the number and arrangement of the teeth other than the specialised anteriorly grooved fangs.

Fairley has introduced the use of *Quadrate* and *Maxillary indices* for the purpose of comparing certain osteological features in the Australian snakes. Phisalix had noted an increase in the quadrate from the Boidae (pythons) through the Proteroglyphae to the Solenoglyphae (vipers). The ratio of the length of the quadrate to that of the skull from the premaxilla to the occiput constitutes Fairley's *Quadrate index*, and it decreases in the Australian reptiles examined

from 4.0 in the diamond snake (*Python spilotes*), 3.45 in the brown snake (*Diemenia textilis*), 3.1 in the copper head (*Denisonia superba*), 2.9 in the black snake (*Pseudechis porphyriacus*), 2.5 in the tiger snake (*Notechis scutatus*), to 2.0 in the death adder (*Acanthophis antarcticus*). He has also instituted a comparison between the maxillary indices and the degree of possible forward rotation of the fangs in the same species. The *maxillary index* is obtained by dividing the length of the skull, measured from the occiput to the premaxilla, by the length of the superior maxilla. There is a transition from a maxillary index of 1.5 in the diamond snake to 3.72 in the death adder, and this last species shows a considerable amount of forward rotation of the fangs during biting.

Fairley also discusses the significance of the inter-fang measurements — increasing distance between the fangs being met with in the more deadly snakes. The average measurement is largest in the death adder (1.6 cm.) and smallest in the brown snake (0.9 cm.). In all species the length of the fangs also tends to increase as the distance between them widens. In the poisonous snakes under investigation the average number of teeth in the upper and lower jaw is least in the death adder and greatest in the brown snake and copper head.

The actual mechanism of biting is fully discussed and analysed, and the function of the muscles concerned confirmed by electrical stimulation. Among the Australian snakes under review the death adder is placed first in biting efficiency, the brown snake last, while the tiger, copper head and black snakes occupy an intermediate position. These snakes appear to form a series linking up at the one end (the death adder) with the vipers and at the other with the non-poisonous aglyphous colubridae.

Dr. Fairley's third paper, written in association with Miss Beryl Splatt, deals with the venom yields of the common Australian venomous snakes. In this, several important points are cleared up. It appears that after biting once or several times there is generally an appreciable amount of venom left in the gland, which may be expressed by "milking." For example, a tiger snake with an average total yield of 43.5 mgm. gave 29.3 mgm. during biting and 14.1 from milking. In death adders the average total yield was 79.1 mgm., of which 57.6 mgm. were given in biting and 21.6 in "milking." A snake which has recently struck may still be dangerous, for with both these species large yields

were obtained in many instances from a second bite immediately after the first, and in some a further amount was obtained from a third bite. The yields of individual snakes in a species were found to exhibit wide variation. The size of yield of venom for any individual reptile appears to be closely related to the length of the snake, its weight and the distance between the fangs. For the death adder the average maximal yield during captivity was 78.2 mgm. of dried venom, the highest individual value being 205 mgm. For the tiger snake the average maximal yield was 47.2 mgm. and the highest individual value 155 mgm. For the copper head the average maximal yield was 24.9 mgm. for Dr. Fairley's series and 40.1 mgm. for a larger series collected at Mount Gambier somewhat later. The maximal individual yield for this snake was 189.6 mgm.

For the black snake the average maximal yield was 47.2 mgm. in a small series of snakes, the highest individual yield being 74.7 mgm. A later series gave an average yield at the first milking of 11.3 mgm. From brown snakes no venom was obtained even on milking.

Dr. Fairley's fourth paper deals with the value of ligature as a therapeutic procedure which he investigated experimentally in sheep. With black snake venom Sir Charles Martin had shown that 6 to 10 times the fatal dose could be administered to a rabbit if the circulation of the limb into which the venom was injected were blocked completely for 20 minutes. He also showed that the value of the method was dependent on a thermolabile constituent of the venom, for, if the "thrombase" in the venom were destroyed by heating to 75° C., the only effect of ligature was to delay the time of death. Fairley's experiments suggest that the absorption time for tiger snake venom after natural bite, i.e., the time required for the absorption of a lethal dose into the circulation, does not exceed two minutes. Hence ligature and excision to be effective must be applied within this time. The result of ligature in experiments in sheep with death adder and copper head venoms in which thrombase was shown to be absent was only to prolong and not to save life. In both sheep and goats injected with tiger snake venom ligature failed to save life even when only a single certainly lethal dose was injected. Dr. Fairley relates the failure of ligature in the sheep to a low subcutaneous-intravenous index, i.e., to the relatively low degree of "thrombase" activity of the venom for this species. The toxicity of the Australian elapine venoms under consideration has been deter-

mined for the sheep, and with some venoms for the goat, also by both intravenous and subcutaneous injection. For the sheep by subcutaneous injection the certainly killing dose is, for tiger snake 0.01, for death adder 0.25, for copper head 0.1, for the black snake 0.8, for the cobra 0.25, and for Russell's viper 1.85 mgm. per kilo, and the subcutaneous intravenous index is 2.0 for tiger snake venom, about unity for death adder, copper head and cobra venoms, and 5.0 for Russell's viper venom. Dr. Fairley concludes that before the results of animal experiments on ligature can be transferred to man the efficacy of ligature should be established in a series of animals. His experimental findings are unfavourable to ligature as a therapeutic measure apart from its immediate value in preventing absorption while excision is being rapidly carried out.

Publications.

FAIRLEY, N. HAMILTON:

"The Present Position of Snake Bite and the Snake Bitten in Australia."

Medical Journal of Australia, March 9th, 1929.

"The Dentition and Biting Mechanism of Australian Snakes."

Medical Journal of Australia, March 9th, 1929.

FAIRLEY, N. HAMILTON, and
SPLATT, BERYL:

"Venom Yields in Australian Poisonous Snakes."

Medical Journal of Australia, March 16th, 1929.

FAIRLEY, N. HAMILTON:

"Criteria for Determining the Efficacy of Ligature in Snake Bite."

Medical Journal of Australia, March 23rd, 1929.

Five other papers in this symposium were contributed by Dr. Kellaway—four of them being devoted to the accurate estimation of toxicity of the venoms of the tiger snake, copper head, and death adder, and of a rare snake allied to the black snake (*Pseudechis guttatus*). In these attention has been paid to differences in toxicity by intravenous

and subcutaneous injection, to variation in toxicity in different species (a large number of species being used as experimental animals), and finally to the elimination as far as possible of individual variation within the species for which the certainly lethal dose was being determined. The main importance of these studies lies in the fact that estimations of toxicity on many species give more valuable information in regard to the toxicity of the venom for man than do observations on a single species, the certainly lethal dose for man being of the order indicated by the limits of the values of the certainly lethal doses for a large number of other species. They have a further value in enabling us to select suitable animals for the titration of antivenines and for the study of venoms by fractionating them in various ways.

Tiger snake venom administered subcutaneously has a certainly lethal dose of about 0.005 mgm. per kilo of body weight in the horse, 0.02 mgm. in the guinea pig and monkey, 0.045 mgm. in the rabbit, but a larger dose is required in the rat and the mouse. The range of fatal dosage indicated in 7 species studied, or 9 including the sheep and the goat, is from .005 to 0.4 mgm. per kilo. Individual variation in animals of a single species is definitely related to the size of the animals, a smaller dose per kilo being fatal in larger animals. For this, though not for other venoms, it seems likely that body weight is almost as important as species differences are in determining toxicity, since larger kinds of animal are, generally speaking, more susceptible than smaller ones. It seems likely then that the lethal dose of tiger snake venom for man lies nearer to that of the horse and sheep, and may be of the order of 0.005 to 0.01 mgm. per kilo. General considerations indicate that it is somewhat larger than this, for if this were the case only about a milligram of this venom would be required to kill an adult man of average size.

This venom when injected intravenously is, as is well known, much more toxic on account of its coagulant action. This difference between subcutaneous and intravenous injection is most evident in the rabbit, for which a value of 22.5 for the subcutaneous intravenous index was obtained. For other species the index was much smaller.

The venom appears to vary somewhat with the condition of the reptiles. Venom collected from starved snakes which were heavily infested with fluke was somewhat less toxic than that collected from reptiles which were in good condition.

The symptoms exhibited in different species were very uniform and displayed the neurotoxic, haemolytic and thrombotic effects of the venom.

The study of copper head venom revealed its high potency for most of the species investigated, the certainly lethal doses ranging from less than 0.02 mgm. per kilo in the horse to rather more than a milligram per kilo in the rat and mouse. The guineapig is the most susceptible animal, the certainly lethal dose being only three times as large as that of tiger snake venom. The venom of this snake is of peculiar interest, since the snake is very common in this state, and since the venom has not previously been investigated. It has no thrombotic action—the subcutaneous-intravenous index for most species being about 2.5. Its powerful neurotoxic action overshadows its local and haemolytic effects.

The study of the venom of the death adder shows that its toxicity varies in different species from 0.04 mgm. per kilo in the horse to about 0.4 and 0.7 mgm. per kilo in the rat and mouse. The subcutaneous-intravenous indices vary from unity to 2.5 and the venom has no thrombotic action in any species. The certainly lethal dose for man is probably of the order of 0.025 to 0.15 mgm. per kilo. The venom is complex in action, exhibiting neurotoxic haemorrhagic and haemolytic activity.

The venom of *Pseudechis guttatus* has not previously been investigated. It has been shown to contain thrombase, haemolysin, haemorrhagin and neurotoxin. The certainly lethal dose for most of the species studied lies between 0.6 and 0.8 mgm. per kilo, and the subcutaneous-intravenous index is about 1. The venom is more haemolytic than that of the tiger snake (*Notechis scutatus*), and has less thrombotic activity in the species investigated than the venoms of *Notechis scutatus* and *Pseudechis porphyriacus*. Its haemorrhagic action is considerable, and the pathological changes produced by subcutaneous injection of the venom in small animals, particularly in the guineapig, resemble those produced by diphtheria toxin. The venom, like that of other Australian venomous snakes, has a powerful stimulant action on plain muscle.

The final paper of the symposium is concerned with the demonstration of the absence of thrombotic activity in the venoms of the copper head and death adder by the injection into laboratory animals of very large doses intravenously

without producing intravascular coagulation. The venoms were also tested with fowl plasma and with citrated and oxalated mammalian plasmas *in vitro*, and only exhibited coagulation with very high concentrations of venom acting on very small amounts of plasma. That these two venoms also possess feeble anti-coagulant powers was demonstrated by the method devised by Lamb, namely, the addition of calcium chloride to citrated and oxalated plasma which have been incubated with varying doses of the venoms. The anti-coagulant activity of the venom is not destroyed by heating the venom, but somewhat enhanced. The subsequent reaction of mammalian plasmas with coagulant venoms is also impaired by incubation with these venoms—a phenomenon which is due either to proteolytic ferments in the venoms or possibly to bacterial action.

The Action of the Australian Snake Venoms on Plain Muscle.

Dr. Kellaway has described a new phenomenon in the action of these snake venoms on isolated smooth muscle. This is wholly different from the effects produced by the toxins of *Vibrio Septique* and *B. welchii* described by Buttle and Trevan. The reaction obtained with the plain muscle of the guineapig resembles closely the anaphylactic reaction of sensitive plain muscle both in its time reactions and in the ease with which the muscle is desensitised with any one snake venom to a subsequent treatment with the same venom or any other of the group. Some venoms are active in concentrations of 1 in 5 to 1 in 10 millions. The effect is non-specific, one venom desensitising to others. Experiments with antivenine kindly provided by Dr. Morgan show that, though some neutralisation of the stimulant property occurs both for the venom against which the antivenine was prepared and also to a much lesser extent against others, this neutralisation is not so specific as that of the toxic properties of the venom. The action of snake venom appears to be on the muscle itself, and not on the end plates, and desensitisation is permanent, though the subsequent reaction of the muscle to other stimuli is not impaired. Sensitive plain muscle can apparently be desensitised to snake venom without impairing its sensitiveness to the specific anaphylactic antigen with which it has been sensitised. The reaction with snake venom has been shown not to be due to the production of a stimulant substance such as histamine, for contraction and not relaxation is produced by venom in the uterus

of the rat. Densitisation with snake venom does not impair the response of the plain muscle to the toxin of Vibrion Septique, a sample of which was kindly given us by Dr. Trevan, of the Wellcome Physiological Research Laboratories, but immediately after reaction to this toxin the plain muscle does not respond either to snake venom or to any other stimulus. There is some evidence of the presence of this stimulant substance in the venoms of the Cobra and Daboia, for they may be used to desensitise the plain muscle. The stimulant substance is present in the secondary proteose fraction of the venoms and behaves like neurotoxin in its destruction by prolonged heating.

Dr. Kellaway is at present engaged on studies concerning active immunity against snake venoms, on the nature and toxicity of the venoms of some of the rarer snakes, and on the venom of *Latrodectus hessellti*—the common red-backed spider. With Miss Freeman attempts are being made to fractionate the venoms of the copper head and death adder with a view to further study of their toxicology.

KELLAWAY, C. H.:

“A Preliminary Note on the Venom of the Australian Copper Head (*Denisonia superba*)—Its toxic effects in the common laboratory animals.”

Medical Journal of Australia, March 16th, 1929.

“A Preliminary Note on the Venom of *Pseudechis guttatus*.”

Medical Journal of Australia, March 23rd, 1929.

“The Venom of *Notechis scutatus*.”

Medical Journal of Australia, March 16th, 1929.

“Observations on the Certainly Lethal Dose of the Venom of the Death Adder (*Acanthophis antarcticus*) for the Common Laboratory Animals.”

Medical Journal of Australia, June 8th, 1929.

“The Action of the Venoms of the Copper Head and the Death Adder on Coagulation.”

Medical Journal of Australia, June 8th, 1929.

“The Action of Australian Snake Venoms on Plain Muscle.”

(In the Press.)

Bacteriophage.

Dr. F. M. Burnet has continued work on several problems in connection with bacteriophage phenomena with the assistance, since August, 1928, of Miss McKie.

The relationship between phage activity and the antigenic structure of the organism attacked has supplied material for two papers, one in collaboration with Miss McKie. Work done at the Lister Institute showed the importance of the so-called "rough" change in bacteria in modifying their reaction to phage. Frequently the effect of a bacteriophage on a normal culture is to produce "rough" strains which resist the action of the phage. Conversely normal smooth strains may be derived from rough cultures by the use of suitable phages. It was suggested that what determines the activity of bacteriophage against any given bacterium is the antigenic configuration of the bacterial surface (or more definitely the heatstable agglutinogenic structure). This hypothesis if established should have some significant bearing on general immunological theory, and further evidence in support of it has been sought in two directions.

In the first place cultures derived by the action of phage which showed a sharp distinction from the parent strain in their behaviour to phage but no gross antigenic change were more closely studied. No distinction could be made out by the use of the methods of reciprocal agglutinin absorption—the most sensitive immunological test available—but, using phage absorption methods, clear evidence of changed surface configuration was obtained. The results did not add any direct confirmation to the general hypothesis, but, if the hypothesis is accepted, they show clearly that bacteriophage methods supply a more delicate test for structural change in bacteria than any other current immunological procedure.

Secondly, staphylococci and their phages were used in an attempt to see whether the relations between phage sensitivity and antigenic structure established for bacilli of the intestinal group held for these totally dissimilar organisms. A great deal of work was expended on staphylococcal lesions in man in order to obtain suitable phages, but active phages were found to be extremely rare. Two moderately active and three weak phages were obtained, but no suitable material for the antigenic analysis of staphylococcal variants that was contemplated.

A nonpathogenic staphylococcus was, however, isolated from animal faeces, and from similar sources a number of distinct staphylococcal phages were obtained capable of lysing this strain. A study of the variants of this organism under the influence of different phages gave interesting results. It was shown that each of four bacteriophage types was related to certain definite antigenic components of the organism, and that when one of these components was lost there was a corresponding change in the reactions of the strain toward bacteriophage and in its antigenic power.

Incidental to other work on bacteriophage a method of following the course of phage multiplication in broth cultures has been developed. There has been and still is an extensive controversy over what actually happens in the first stages of phage action. One school holds that a phage particle penetrates a bacterium and multiplies within it, producing a variable number of descendant particles which are suddenly liberated when the cell dissolves. Opponents of this view consider that lysis and phage multiplication are not necessarily interdependent. The principle of this new method is to isolate numbers of single phage particles in small volumes of broth culture and at frequent intervals to plate the whole volume (including all the descendants of the single particle) on agar. In this way it has been shown that the first increase is always sudden. Up to a certain period all platings show the presence of one or no particles, then in some there appear, say, 30 plaques, but never intermediate counts that would be expected were multiplication a regular doubling in number such as occurs in bacterial growth. The only explanation that satisfies the facts is that sponsored by d'Herelle, namely, that the observant multiplication of phage always results from lysis of sensitive bacteria.

Miss McKie is at present engaged in an attempt to apply the principles developed in earlier work on other organisms to the phages that act on *B typhosus* with a view to a closer analysis of the types of phage found in patients with typhoid fever.

Staphylococcal Toxin.

The results of the Bundaberg enquiry have reopened interest in the toxic products of the staphylococci, and a good deal of work under a grant from the Department of Health, Commonwealth Government, has been done on the

specific toxin produced by these organisms. The toxin has been studied previously by a few observers, but it has escaped any general discussion in the literature of bacteriology probably on account of the difficulty of preparing consistently active toxins. The present work has shown that strong toxins can be obtained by growing a suitable strain in broth in an atmosphere containing 20% of carbon dioxide. Filtrates from 8-day cultures grown in this way possess a toxicity that can be manifested in at least three fashions (1) by haemolysing the red blood cells of the rabbit, (2) by producing necrotic lesions when injected intradermally into the skin of the rabbit, (3) by killing rabbits acutely when injected intravenously. All these activities can be neutralised by a single antiserum, and quantitative experiments have shown that in all probability the three types of toxic activity are all manifestations of a single antigenic substance. The part played by this exotoxin in lesions produced by staphylococcal infection is under investigation. There is direct evidence of its importance in the acute killing of rabbits by staphylococci and a suggestion that it plays a large part in determining the localisation of staphylococcal lesions in the kidneys. It is hoped to carry out some investigations on the possible part played by the toxin in the acute staphylococcal infections of children such as osteomyelitis. A brief survey of the pharmacological properties of the toxin was undertaken by Dr. Kellaway. It was shown that rapid death following intravenous injection in rabbits was due primarily to failure of the heart to maintain the circulation, probably resulting from a direct toxic action on the muscle fibres. The great rapidity of action of this substance—rabbits may be killed in two minutes—marks it off sharply from most other bacterial toxins.

Müller's Phenomenon.

In the course of the investigations into the Bundaberg fatalities of January, 1928, a peculiar appearance was observed on blood agar plates spread with the specific staphylococcus. This was recognised as the phenomenon of distant punctate haemolysis described by Müller in 1927, and a short investigation into the conditions necessary for its production was carried out. It was concluded that the discrete areas of haemolysis resulted from the activation of a haemolysinogen produced by the staphylococci. This activation usually occurs only when the haemolysinogen comes into contact with a complex of a labile

serum constituent and some entity present in meat extract. Each such complex then acts as a source from which an active haemolysin can diffuse.

The phenomenon was obtained with all the pyogenic staphylococci tested, but does not seem to be related to the production of the well-known antigenic haemolysin by these bacteria.

Publications.

BURNET, F. M.:

“Observations on Müller’s Phenomenon. Distant Punctate Haemolysis of Blood Agar by Staphylococci.”

Aust. Jl. Exp. Biol. and Med. (1928), Vol. V.,
p. 205.

“Further Observations on the Nature of Bacterial Resistance to Phage.”

(In the Press).

BURNET, F. M., and

McKIE, MISS:

“Type Differences Amongst Staphylococcal Bacteriophages.”

Aust. Jl. Exp. Biol. and Med. Sc. (1929), Vol. VI.,
p. 21.

BURNET, F. M.:

“A method for the Study of Bacteriophage Multiplication in Broth.”

Brit. Jl. Exp. Path (1929), Vol. X., p. 109.

“Bacteriophage in its Clinical Aspects.”

Medical Journal of Australia, March 30th, 1929.

“The Exotoxins of Staphylococcus Aureus.”

(In the Press.)

Role of CO₂ in Bacterial Metabolism.

The work on Staphylococcal toxins showed the importance of growing the bacteria in an atmosphere containing a proportion of CO₂ if powerful toxins were to be produced. The effect of CO₂ is even more marked if staphylococci are

grown on the surface of agar. A powerful toxin is produced in the presence of 20% of the gas, but practically none if the CO₂ is absorbed as it is produced. The working hypothesis has been adopted that this effect is due to the influence of CO₂ on the intracellular pH of the bacteria, and experiments are being made to determine the influence of such changes on a number of bacterial activities, particularly toxin production and bacteriophage lysis.

Poliomyelitis.

Dr. Burnet and Dr. Jean Macnamara have collaborated in work on poliomyelitis under a grant from the Commonwealth Government. The use of convalescent human serum in the treatment of pre-paralytic cases of infantile paralysis requires the provision of suitable methods of obtaining and storing the serum. The methods used for this purpose by the Commonwealth Serum Laboratories have not previously been adopted, and it was felt that direct experimental evidence of the potency of the serum as prepared was required. This has been satisfactorily accomplished, and both Group 1 (from recent cases) and Group 2 sera (from cases paralysed in 1925) have been shown to be actively virucidal. Quantitative experiments with monkeys are limited by the difficulty of procuring the animals, but as far as the small number of experiments allow it can be said that the two types of sera are of about equivalent potency.

The Biochemical Department.

The special researches carried out in this department under the direction of Mr. H. F. Holden have mainly been concerned with the constitution of proteins, especially of globins derived from the haemoglobins of mammalian blood and with the changes which accompany denaturation.

Mr. Holden and Miss Freeman have studied the stoichiometric relation between haematin and globin, using the spectro colorimeter previously described by the former to estimate the amount of methaemoglobin produced from globin by the addition of known amounts of haematin. The methaemoglobin was converted into oxyhaemoglobin by treatment with a reducing agent, followed by atmospheric oxygen. The weight of "globin" present was determined by heat-coagulation in the presence of saturated

ammonium sulphate. They were able to show that the chemical equivalent of globin in reconstituted haemoglobin was the same as in natural haemoglobin—651 parts of haemin being equivalent to 16,050 parts by weight of globin. Using methods different from those employed by Wu and Lin, they were able to confirm the observations of these authors that if methaemoglobin were converted to acid haematin and neutralised at once almost all the acid haematin reverted to methaemoglobin, whereas, in the case of oxyhaemoglobin, only 2-3 reversion could be obtained. The optical activities of globin and of denatured globin were shown to be very different. Such a change in optical activity as occurs in the case of ox globin for example from -13° to -71° or -73° , suggests that a profound change in chemical structure accompanies denaturation. Finally, using spectro photometric titration, they showed that denatured globin combines with six times as much reduced haematin to form haemochromogen as globin does to form haemoglobin.

In a second paper Mr. Holden and Miss Freeman have determined spectro-photometrically the relative dissociation of some simple haemochromogens, and have determined the combining ratio of reduced haematin to protein in several protein haemochromogens. They have described the preparation of the parahaematin of denatured egg albumin, casein and of four methyl iminazole, and have investigated the effect of formaldehyde and of nitrous acid on the formation of haemochromogens and parahaematin.

The spectro-photometer used in these researches was very kindly lent by Professor W. A. Osborne, of Melbourne University.

Mr. Holden has also studied the antigenic properties of globin. Guineapigs injected subcutaneously with horse globin did not react when tested a month later by the intravenous injection of the protein. In experiments with isolated plain muscle after first desensitising with serum and stroma proteins, some sensitivity to a substance in the solution of horse globin used was detected when the subcutaneous dose used for the sensitising injection had been large. Owing to the difficulty of preparing globin free from traces of other proteins, it was considered that this antigenic substance was not globin itself.

Publications.

HOLDEN, H. F., and

FREEMAN, M.:

“On Globin and Denatured Globin.”

Aust. Journ. Exper. Biol. Med. Sc. (1928), Vol. V.,
p. 213.

“On Haemochromogen and Some Related Compounds.”

Aust. Journ. Exper. Biol. Med. Sc. (In the Press.)

HOLDEN, H. F.:

“Anaphylactic Experiments with Globin.”

Aust. Journ. Exper. Biol. Med. Sc. (1928), Vol. V.,
p. 285.

Mr. Holden is also engaged in an investigation of the effect of denaturation on the ultraviolet absorption spectrum of proteins. Professor Hicks, of Adelaide University, is collaborating with Mr. Holden in this research, and has generously made his own private instrument available for this work. In the proteins so far examined no changes in their ultraviolet absorption curves have been observed to follow denaturation, so that for these proteins at least the amino acid groupings responsible for optical activity and for ultraviolet absorption are probably separate and distinct.

Further studies are in progress on the effect of denaturation on the optical rotatory dispersion of proteins, and attempts are being made to prepare meta-proteins of constant optical rotatory dispersion. Experiments are also in progress on the relationships of the proteins in salt free sera and on the behaviour of certain proteins towards metallic salts and various denaturing agents.

Apart from these special studies, the workers in this department have been able to co-operate in other researches. Miss Freeman is commencing some studies on the Australian snake venoms—on their chemical composition—on their various enzyme activities, and, as already mentioned, on the fractionation of venoms to determine the nature of the active principle or principles present. Mr. Holden is collaborating with Dr. Kellaway in the preparation of the factors involved in blood coagulation for studies on the coagulant and anticoagulant activities of these venoms.

Basal Metabolism.

Dr. J. F. Chambers has put on record some observations on this subject based on over a thousand tests on 263 private and 410 hospital patients carried out during the last six years. In these he has used the Douglas bag, the Haldane gas analysis apparatus and the Du Bois surface area chart and standards.

He has also recorded three groups of observations on normal people, —18 on University students at Melbourne with an average B.M.R. of -6.5% , 32 on hospital patients admitted to the Melbourne Hospital for minor uncomplicated surgical disabilities with an average B.M.R. of $+1.7\%$, and 12 of similar type studied in England at St. Thomas's Hospital with an average B.M.R. of $+8.6\%$. His results suggest that, as has been noted by other observers, normal metabolism in this country appears to be on a slightly lower plane than in England. The American Du Bois standards can apparently be adopted in Victoria with the acceptance of $\pm 0\%$ as the absolute theoretic normal. The low values obtained with medical students probably depends on a special effort by the subjects to relax and are similar to the low values obtained elsewhere when intelligent trained subjects have been studied.

In only 3 of 99 cases of cardiac neurosis were the basal metabolic rates above $+15\%$, thus supporting the findings of Boothby, Sandiford and others that rapidity of heart action *per se* does not materially raise metabolism. The effect of under nutrition, prolonged rest and long exhausting illness in lowering the metabolic rate are discussed.

Dr. Chambers' series includes 213 persons with thyrotoxicosis—19 of these were toxic adenomas of an average age of 41, with an average B.M.R. of 30% before treatment, and 162 were exophthalmic goitres with an average age of 34 years and average B.M.R. of 43% . The effects of treatment with Lugol's iodine solution in this series of cases are discussed, and also the incidence of cardiac involvement, periorbital oedema, gastro-intestinal crises and glycosuria. Thyrotoxicosis in Australia appears to differ somewhat in type and severity from that met with in America. With us there are fewer fulminating cases, and fewer gastro-intestinal crises, and iodine hyperthyroidism is less common. Metabolic rates are rarely very high, only one in this series being in excess of $+100\%$, the next highest being $+85\%$.

The results and complications following operation in 130 patients with thyrotoxicosis are discussed. Low metabolism after operation does not necessarily indicate hypothyroidism.

The determination of the basal metabolic rate is of great value in a large group of conditions which simulate thyrotoxicosis, 210 patients in this series (84 of whom had enlarged thyroids) being placed in this category.

There were 23 patients with myxoedema with basal metabolic rates ranging from -14% to -43% . The diagnosis of this condition and variability of tolerance for thyroid in treatment are discussed. Improvement in renal function following thyroid treatment was noted in several cases. 73 patients in this series were investigated in regard either to a subthyroid condition or to pituitary disorder. There were 20 cases of non-toxic goitre, with some evidence of secretory deficiency. Finally there were two patients with *polycythaemia vera* with high rates, and two with myelogenous leukaemia under X-ray treatment, which illustrated the high metabolic rates met with in the active stage of this disease.

CHAMBERS, J. F.:

"Basal Metabolism—A Clinical Study."

The Medical Journal of Australia, Dec. 1st, 1928.

Hydatids.

Dr. N. H. Fairley and Dr. R. J. Wright-Smith have completed an extensive study of the morphology of hydatid cysts in sheep, oxen and swine, with special reference to daughter cyst formation. They observed the incidence of degeneration in 6497 sheep cysts, in 929 ox cysts and in 727 pig cysts. In 43 examples of early endogenous daughter cyst formation there was no example of degeneration or rupture of the parent cyst and the adventitia was normal in 39 instances. They regard the degeneration in old mother cysts as a secondary phenomenon occasioned by the growth of young endogenous daughter cysts. Their observations on the early stages of endogenous daughter cyst formation make it clear that these daughter cysts do not originate under conditions menacing the life of the cyst.

In 162 examples of exogenous daughter cyst formation, the mother cyst was ruptured in nearly half, but the adventitia was normal in about 80%. Degeneration of the original mother cyst depends on its mechanical separation from the adventitia by daughter cysts. No support was found for the view that daughter cysts originate as external herniations through the adventitia.

Pseudo daughter cysts were studied in pig cysts where they originate as hyaline degenerations of the laminated layer. Failure to recognise their true nature appears to have led to the commonly accepted view of the intracuticular origin of daughter cysts.

The study of this large series of cysts support Dévé's view that the most common source of endogenous daughter cyst formation is by vesicular evolution of the scolex.

FAIRLEY, N. HAMILTON, and
WRIGHT-SMITH, R. J.:

"Studies in the Comparative Pathology of Echinococcus Granulosus (Batsch), with Special Reference to Daughter Cyst Formation."

Journal of Pathology and Bacteriology (1929),
Vol. 32, p. 308.

Hydatids,

The Intradermal Test.

A careful analysis of all the skin tests carried out at the Institute until November, 1926, has been carried out by Dr. Keith D. Fairley (Clinical Research Scholar of the University of Melbourne). He found that 77% of patients harbouring uncomplicated cysts and 92.6% of those with ruptured or suppurating cysts gave an immediate response. Absence of an immediate response correctly indicated the absence of hydatid disease in 96.8% of cases. A positive delayed response was found in 56% of patients with uncomplicated cysts, and in 26% of those with ruptured or suppurating cysts. Since there were a number of fallacious immediate positive responses, the chief value of the test is in excluding hydatid disease when the result is negative. Though only about half the patients with

uncomplicated cysts gave positive delayed responses, fallacious positive responses were so rare that such responses when they occur are good evidence of hydatid infestation. It is unwise to operate upon the unsupported evidence of a positive immediate response to the intradermal test. The absence of an immediate response months or years after operation in a patient previously showing a positive response is strong evidence of cure if recent rupture of a cyst can be excluded. An immediate or delayed reaction occurring ten years or more after an operation for hydatid disease demands the careful investigation of the patient for further cysts.

FAIRLEY, K. D.:

“The Intradermal Test in Hydatid Disease—A Critical Analysis of its Results.”

Medical Journal of Australia, April 13th, 1929.

Dr. N. Hamilton Fairley, Dr. Keith Fairley, and Miss F. E. Williams, aided by a grant from the Commonwealth Government, proceeded to investigate the cause of the fallacious positive tests met with in the analysis. Some of these unquestionably depended on misinterpretation of the observed result, the tests having been carried out by a number of different observers. One only was found to be due to sensitisation to sheep serum protein—hydatid fluid from sheep cysts being used as a routine for the test. The possibility of pharmacologically active substances in sensitive individuals being responsible for some of the pseudopositives was also investigated. Fifty fluids were tested by Dr. Kellaway, and earlier observations from this Institute were confirmed—only slight activity being found. The use of pharmacologically active fluids for the skin test afforded some indication that pseudopositive responses may occasionally occur from this cause.

One most important cause of misleading positive reactions may occur in patients tested on more than one occasion, namely, the development of local skin sensitisation following the earlier injection or injections. Whereas local active sensitisation was readily produced, general sensitisation was not demonstrated even after a series of injections of hydatid fluid, except in one patient following the injection of saline scolex extract.

Undoubtedly the most important cause of fallacious responses in the skin test is infestation with other helminths. Skin tests with extracts of *T. saginata* and *Ascaris lumbricoides* showed that patients sensitised with these extracts could react with scolex extract. Patients who had been operated on for hydatid disease, and who gave positive immediate reactions with scolex extracts in 74% of cases, gave reactions with *T. saginata* and ascaris in 59% and 23% of cases respectively. On the other hand there were nearly 30% of positive intradermal responses with ascaris extract in a series of patients with no evidence of hydatid disease, and of nine patients with recent or old infestation with thread worms none reacted with either *T. saginata* extract or hydatid fluid. Infestation with tapeworms may, therefore, cause sensitiveness to hydatid fluid and scolex extracts, but infestation with nematodes is a much less likely source of error.

Among the 35 patients who showed fallacious positive immediate reactions there was one with a history of angio-neurotic oedema and three with a recent history of urticaria. *Urticaria factitia*, which, according to Lewis, occurs in 5% of normal people, must be excluded. *Jaundice*, as a cause of pseudopositive reaction, does not appear to be so important as was earlier thought.

More exacting standards and controls for the test are laid down. The antigen used for the test should be standardised by being used on a series of patients in whom there is no evidence of hydatid disease, and on a patient known to show both phases of the response with a suitable hydatid antigen. Standard measurements should be adopted for positive, doubtful and negative results.

The stroke test, introduced by Lewis to determine the reaction of the superficial tissues to slight trauma, should be used as a routine control in all cases tested. No significance should be attached to an immediate reaction occurring in any patient showing a triple response to the stroke test, nor in one who shows a positive or doubtful reaction to the control injection of normal saline solution.

If these tests show that the patient is a suitable subject for the test, a positive immediate or delayed reaction should not be interpreted as a genuine one until infestation with other helminths has been excluded.

FAIRLEY, KEITH D., FAIRLEY, N. HAMILTON, and
WILLIAMS, F. ELEANOR:

“Some Fallacies in the Intradermal Test for Hydatid
Disease.”

The Medical Journal of Australia. (In the Press.)

In anaphylactic studies with extracts of hydatid scolices Dr. Kellaway has shown that extracts in absolute alcohol made with ground up scolices which have already been extracted with pure dry acetone can give rise to sensitiveness, but cannot discharge it. The use of pure dry reagents does not guarantee the absence of host serum protein from these alcoholic extracts. Saline extracts contain in addition to host protein a true anaphylactic antigen of parasitic origin—capable both of sensitising animals and of discharging sensitiveness—causing “shock” in the intact animal or a characteristic contraction of the isolated plain muscle. Though hydatid fluid can be used to elicit an anaphylactic reaction with the plain muscle of animals sensitised with scolex extracts—the sensitiveness of the muscle is not thereby wholly discharged. Conversely, the plain muscle of animals sensitised with hydatid fluid heated to destroy host protein reacts with saline scolex extracts, but is not desensitised thereby, and gives a good response when later tested with hydatid fluid. These observations suggest the presence in scolex extracts of a parasitic antigen other than the antigen or antigens in hydatid fluid.

KELLAWAY, C. H.:

“Anaphylactic Studies with Extracts of Hydatid
Scolices.”

British Journal of Experimental Pathology (1929),
Vol. X., p. 115.

Fluke.

Anaphylactic experiments in which extracts of the liver fluke were used both for sensitisation and testing gave results which fall into line with those obtained with hydatid scolices. There are at least two antigenic substances in these extracts, a true anaphylactic antigen—which is soluble

in water and heat stable, and which shows decreasing solubility in increasing strength of alcohol, and another, probably a lipin, soluble in absolute alcohol, which can be used to sensitise guineapigs, but which is incapable of discharging the sensitiveness of plain muscle. This last substance may possibly be identical with the antigenic substance which is responsible for complement fixation.

KELLAWAY, C. H.:

“Anaphylactic Experiments with Extracts of Liver Fluke (*Fasciola hepatica*).

The Australian Journal of Experimental Biology and Medical Science, Vol. V., p. 273.

In further unpublished experiments, Dr. Kellaway has shown that the anaphylactic reactions of the helminths show a certain lack of specificity, a result which is in close agreement with the results of intradermal skin tests discussed above. Guineapigs sensitised with either *Ascaris*, *T. saginata*, hydatid scolex or fluke extracts were tested by intravenous injections of these extracts or by the reactions of the isolated plain muscle. Guineapigs sensitised with scolex extracts could be killed by the intravenous injection of *T. saginata* extract in doses which were without effect upon normal guineapigs, and the symptoms were indistinguishable from those of fatal anaphylaxis. The plain muscle of animals sensitised with ascaris or saginata extracts reacted with scolex extracts almost as well as with the extract which had been used for sensitisation.

Disease Incidence in the Herbivora.

Last year Dr. N. H. Fairley and Mr. Penrose, B.V.Sc., Superintendent of the City Abattoirs, working under a grant from the Commonwealth Government, carried out a survey of nearly 5,000 cattle, of about 60,000 sheep, and of nearly 2,500 swine. Dr. Fairley and Mr. Penrose have placed on record the findings in regard to the occurrence of hydatid disease in the cattle and pigs, and in the first 11,000 sheep of the survey. The complete analysis of results of this survey in sheep in regard to hydatid, liver fluke, lung worm, cysts of tenuicollis and infective lymphadenitis has just been completed by Mr. E. Southwood, and

the data, together with those on cattle for actinomycosis, tubercle and fluke, will be embodied in a monograph which it is hoped will shortly be published by the Department of Health of the Commonwealth Government.

In a preliminary paper the incidence of hydatid disease is recorded as 16.5% for sheep, 23.9% for cattle, while only a very few swine were found to be infested. The incidence of infestation increases with age, irrespective of sex and breed. This is well illustrated by the incidence in sheep. Under three years of age the average infestation rate was 7.5%, whereas in the older animals it was 26%. In cattle the same rule holds, and a progressive increase was noted from 1½ years of age to 3½ years and onwards. Dr. Fairley and Mr. Penrose have laid great stress on the importance of the institution of more active measures directed towards prophylaxis, more particularly the prevention and elimination of infestation in dogs.

FAIRLEY, N. HAMILTON, and
PENROSE, J. S.:

"A Survey of the Incidence of Hydatid Disease in the
Herbivora and Porcines of Victoria."

The Medical Journal of Australia, Nov. 24th, 1928.

Bilharzia.

Dr. K. D. Fairley and Dr. N. H. Fairley have reported four cases of bilharzia in immigrants from Palestine who were investigated at this Institute. All four were infested with *S. haematobium*, and two showed in addition ova of *S. mansoni* in the urine. All these gave positive complement fixation tests.

The authors regard the active measures adopted by the military authorities and by the Department of Health in confining cases to sewered areas, and effectively treating them as the reason why this disease has not become endemic in Australia, and emphasise the importance of the more insidious danger arising from immigrants who may only develop clinical manifestations of the disease after arrival in the Commonwealth.

FAIRLEY, N. HAMILTON, and
FAIRLEY, K. D.:

"Bilharzia in Immigrants from Palestire."
(In the Press.)

Cancer.

There will shortly be published an analysis of 958 proved cases of malignant disease treated at the Melbourne Hospital between 1921 and 1925. This analysis has been done by Mr. Henry Searby, F.R.C.S., working under a grant from the Department of Health of the Commonwealth Government. The most striking fact which emerges from this study is the necessity for propaganda in order to ensure earlier treatment in patients suffering from cancer.

Excluding all growths which owing to their position were not amenable to radical treatment, there remained 750 cases. Of these, less than 25% came to hospital at a stage where surgery or radiation therapy, or both combined, offered a possible chance of cure. Even with cancers of the skin, only 50% of patients came to hospital while the growth was still localised. Mr. Searby arrives at certain several conclusions in regard to the best methods of treatment in various types of growth. Except in very early cases, growths within the mouth should be treated by excision of the deep cervical glands (whether palpable or not) and radiation, preferably with radium, to the growth itself. The treatment of choice for carcinoma of the lip is a "one stage" excision of the lymphatic field and of the growth itself. This should be done whether the glands are palpable or not, and if both excisions cannot be done in one stage that of the gland bearing area should be done first. Gastrostomy, though it adds to the comfort of the patient, does not prolong life in cases of carcinoma of the pharynx or oesophagus. In most cases of carcinoma of the pharynx radical operative procedures are unjustifiable because of glandular metastases in the mediastinum, and it is very doubtful if they should be used in cancer of the oesophagus. Cancer of the cervix should be treated with radium. Amputation for bone sarcoma is not justifiable if radiation therapy is available. The early removal of an enlarged prostate which is causing symptoms sometimes results in the cure of an early malignant condition.

This analysis brings into prominence the importance of the investigation of all patients over the age of 35 years in whom "indigestion," "constipation or diarrhoea occur without obvious cause." If this were done many more cancers of the stomach and colon might be dealt with at a favourable stage.

SEARBY, H.:

"The Incidence, Regional Distribution and Mortality of Malignant Disease at the Melbourne Hospital during the years 1921-1925."

(In the Press.)

In March of this year the Minister of Public Health of the State of Victoria formed a committee to advise him on the treatment of cancer in this State, on the researches at present in progress, and on the best methods of advancing research, of improving treatment, and of achieving co-ordination with cancer activities elsewhere in Australia. Dr. Kellaway acted as chairman of this committee, which submitted its report early in May.

Oral Sepsis.

Dr. J. M. Lewis and Dr. Arthur Amies are working on the pathological histology of periodontal infections. Both have recently been in Vienna and have familiarised themselves with the methods employed there by Dr. Gottlieb.

In September of last year Dr. Kellaway took part in a symposium on apical infection and addressed a joint meeting of the State Dental Society and the Victorian Branch of the British Medical Association on the bacteriological aspects of this question, the pathological aspects being dealt with by Professor Peter MacCallum and the clinical by Professor F. Wilkinson.

KELLAWAY, C. H.:

"Some Bacteriological Aspects of Apical Infection in its Relation to General Disease."

The Medical Journal of Australia, Feb. 23rd, 1929.

Morbid Anatomy.

Dr. Wright-Smith, who performed this year 449 of 553 routine hospital autopsies, has introduced a number of improvements into the method of recording. Immediately after each autopsy the results are dictated to a stenographer and the records are typed in triplicate—one copy going to the physician or surgeon in charge of the case, one being retained in the Institute, and one being filed with the clinical notes of the case in the hospital records.

623 routine histological examinations for diagnosis of pathological conditions have been made by Dr. C. H. Molli-son and Dr. Wright-Smith. In addition, 366 histological sections of post mortem material were examined.

At a meeting of the College of Surgeons of Australasia, Dr. Wright-Smith, the curator of the museum, gave a demonstration of 23 pathological specimens for the museum—these have been recorded in the Journal of the College.

WRIGHT-SMITH, R. J.:

“Demonstration of Pathological Specimens.”

The Journal of the College of Surgeons of Aus-
tralasia, Nov., 1928.

Dr. Wright-Smith has also recorded two interesting cases—one of recovery in blackwater fever after blood trans-
fusion and another of mirbane poisoning.

WRIGHT-SMITH, R. J.:

“Recovery in Blackwater Fever after Blood Trans-
fusion.”

The Medical Journal of Australia, July 28th, 1928.

“A Case of Mirbane Poisoning.”

The Medical Journal of Australia. (In the Press.)

Routine Work.

At the commencement of the year Dr. Lucy Bryce was appointed to take charge of the routine clinical pathological and bacteriological work of the hospital, which had hitherto

been largely carried out by successive pathological registrars. During the year, the average number of reports sent out each week has been 115, making a yearly total of approximately 6,000. The weekly tests include about 75 microscopical and 30 cultural examinations, and lesser numbers of blood counts, examinations of blood films, estimations of fragility of red blood cells, coagulation and bleeding times, and enumerations of blood platelets, determination of blood groups in donors and patients, and preparation of serum for this purpose, agglutination tests, such as the Widal and Weil-Felix reactions, preparation of vaccines, animal inoculations, determination of pneumococcal types and various others.

Skin tests for allergic sensitiveness in asthma and allied conditions have also been carried out in this department this year. These tests are done once a week, and most patients are tested with twenty or thirty extracts.

The large number of specimens received, many of which require immediate examination, and the very varied nature of the tests which may have to be performed at any time, make it impossible for one person to do all the necessary work satisfactorily, especially when the need arises for detailed investigations in difficult or unusual cases. Dr. Marion Wanliss was, therefore, appointed temporary half-time assistant in September. She resigned in December, and was succeeded in January by Dr. G. R. Osborn as a full-time Resident Assistant Pathologist. Since his appointment he has performed Wassermann and gonococcal complement fixation tests for the hospital, under the initial guidance of Miss Williams. The number of blood specimens received each week is usually over 100, and sometimes as many as 150, so that it has been necessary to do the tests twice weekly.

The systematic filing of the reports of the department has been commenced, so that periodical surveys may be made with a view to improving if necessary the methods adopted, and to recording any facts of value which may emerge from the collected results.

Other routine serological work has been carried out as heretofore by Miss F. E. Williams, and has included complement fixation tests for hydatid disease, 254; Wassermann's, 537; for Bilharzia, 32, and for gonococcal disease, 26.

In the electrocardiographic department the number of patients examined was 338, an increase of 158 over the previous year. Miss Maudsley, with the assistance of Mr. Moseley, has wired one of the wards so that an electrocardiogram can be taken without moving the patients. She proposes to investigate the systems of wiring in use in England while on leave this year, and to wire other wards on her return.

The Basal Metabolic Rate determinations have been facilitated by the arrival of additional apparatus from London. Two hundred and ninety-eight tests have been performed this year.

Miss Maudsley was also responsible for the photographic work both of the Hospital and the Institute, which involved a large number of macroscopic and microscopic photographs.

The work of the bio-chemical department has been heavy this year, over 5,000 specimens having been examined. Miss Marjorie Shannon, who has been helping Miss Splatt in a voluntary capacity for two mornings a week, has recently resigned. Her assistance has been invaluable, and will be very much missed.

The usual routine tests have been performed, including 756 urea concentration tests, 1,110 blood urea estimations, 558 blood sugar estimations, and 234 Van den Bergh Reactions and Fouchet Tests. The fractional test meals have shown a marked increase, 440 having been performed this year, as compared with 347 last year.

Other tests which have been performed this year in large numbers include the estimation of sugar and chlorides in the cerebro-spinal fluid and the colloidal gold reaction. The estimation of cholesterol in blood as a guide to renal damage has been used in a small series of cases. It is highly desirable that other tests, such as the determination of lead in urine, should be carried out, but it has been impossible to start this work during this year through lack of time and assistance.

Dr. Wright-Smith was responsible for the conduct of 214 Casoni Reaction tests—21 positive results and 193 negative have been recorded.

The Museum.

The Museum, under the care of Dr. Wright-Smith, has again proved its usefulness during the year. It has been largely used by University teachers and clinical lecturers, and a series of tutorials in pathology for the M.S. degree was conducted there by Dr. C. J. O. Brown. Various improvements in arrangement have been made, and a number of interesting specimens have been added during the past year, including myxocarcinoma of the palate, multiple jejunal ulcers following gastrojejunostomy, colitis polyposa, alveolar hydatid of the liver, teratogenous carcinoma of the bladder, syphilis of the testis, acute suppurative oophoritis, the uterus from a septic abortion due to *B. welchii*, pneumococcal meningitis, mandibular cyst, adamantinoma, and an angio-endothelioma of the clavicle (Ewing). We are particularly indebted to Dr. C. H. Mollison, Dr. Roy Chambers, Mr. H. R. Dew and Mr. B. Kilvington for the gift of valuable specimens.

Teaching.

During the year courses of lecture demonstrations in elementary bacteriology and in clinical pathology were given to fourth, fifth and sixth year students by Dr. Kellaway, Dr. Burnet, and Dr. Wright-Smith.

The Library.

The Institute Library, which was founded in 1924 by the Edward Wilson (The Argus) Trust, has become increasingly useful as the gaps in our series of journals are filled. In this work it is a pleasure to again acknowledge our indebtedness to Miss K. Baverstock, the Librarian of the National Institute of Medical Research, London, who, as in previous years, has helped us greatly in procuring missing numbers and volumes. Our thanks are also due to the following for gifts of periodicals or books:—Miss Danks, Dr. N. Hamilton Fairley, L'Academie royale de Medecine de Belgique, the Commonwealth Department of Public Health, the Council of Scientific and Industrial Research, the National Institute of Medical Research (London), la Société royale des Sciences médicales et naturelles de Bruxelles, the Rockefeller Institute (New York), and the Royal Society of New South Wales.

BIO-CHEMICAL DEPARTMENT—ENDOWMENT ACCOUNT.

To Balance brought forward from 30th June, 1928			£8,118 12 6			By Bank Fee for Collecting Interest			£1 0 0		
Interest on Investments			£396 1 3			Balance—			£500 0 0		
Donation, British-Australasian Tobacco Co. Ltd.			50 0 0			C'wealth Ins. Stock, 5% Vic. Govt. Ins. Stock, 5½%			140 0 0		
Other Donations			27 16 6			City of Melb. Deb., 5½% Melb. & M. Bd. Wks., 4%			807 12 2		
						Melb. & M. Bd. Wks., 6½%			1,218 4 3		
						Mortgage, M. Anthony, 6%			1,952 11 1		
						Mortgage, Montgomery, 7%			2,550 0 0		
						Deposit at Call, Goldsborough, Mort, 5%			300 0 0		
						Melb. Harbour Trust Debs., 5½%			600 0 0		
						Current A/c., Bank of N.S.W.			500 0 0		
									23 2 9		
									8,591 10 3		
									£8,592 10 3		

LIBRARY ACCOUNT.

To Balance brought forward from 30th June, 1928			£2,000 0 0			By Books, Journals and Bookbinding			£123 5 2		
Interest on Investments			130 0 0			Repayment to Working A/c.			6 14 10		
						Balance—					
						C'wealth War Bond, 6%			£1,000 0 0		
						Mortgage, Montgomery, 7%			1,000 0 0		
									2,000 0 0		
									£2,130 0 0		

To Balance brought forward from June, 1928	£1,150	5	11	By Salaries and Wages	£1,224	16	3
Donation, Edward Wilson Trustees	1,000	0	0	Materials	22	19	11
				Apparatus	195	6	3
				Fittings and Equipment	128	10	0
				Sundries	0	15	4
				Balance—			
				Cash with Agent-Gen..			
				London	£58	9	8
				Bank of N.S.W., Current A/c.	519	8	6
					577	18	2
	£2,150	5	11		£2,150	5	11

I have to report that I have completed the audit of the books and accounts of the Institute for the period ended 30th June, 1929. I have verified all receipts and have had vouchers produced for all disbursements. All information and explanations required have been given. The statement is a correct statement of receipts and expenditure as revealed by the books of the Institute.

W. M. JARVIE, F.F.I.A., Auditor.

